Severe Bradycardia Caused by a Single Dose of Lithium

Manpreet S. Sabharwal, Narender Annapureddy, Shiv Kumar Agarwal, Natraj Ammakkanavar, Vijay Kanakadandi and Girish N. Nadkarni

Abstract

Lithium is used as a mood stabilizer in patients with manic-depressive disorder. It is a drug that requires close monitoring due to its narrow therapeutic window and many side effects. There are several case reports of lithium side effects and toxicity occurring even at the therapeutic levels. Cardiac toxicity is observed in approximately 5% of patients; however, severe bradycardia caused by a single dose of lithium is exceedingly rare. We herein report a case of severe symptomatic bradycardia in a young man that occurred after a single dose of lithium. This case emphasizes the need to closely monitor patients when initiating therapy, even before the lithium levels are high enough to be detected.

Key words: lithium, cardiotoxicity, bradycardia

Introduction

Lithium is used as a mood stabilizer in patients with various affective disorders. It is known to cause various cardiac disorders, including conduction abnormalities. The mechanisms underlying these conduction defects are not understood. A wide range of lithium toxicities have been observed, from severe bradycardia to arrhythmias. Direct effects on the sinus node and thyroid function abnormalities have been postulated to underlie these side effects. However, most previous cases of conduction abnormalities occurred in the setting of chronic lithium therapy or in patients receiving toxic levels of lithium. Our case highlights the potential for acute cardiotoxicity induced by a single dose of lithium and the need for vigilance during the administration of this potentially toxic medication.

Case Report

A 27-year-old man with history of bipolar disorder was admitted for suicidal ideation one day previously. The patient’s history included polysubstance abuse with marijuana and alcohol use one day prior to admission and a suicidal attempt one year previously. He had no significant family history of any cardiac conditions. The patient reported non-adherence with psychiatric medications. An initial examination revealed normal vital signs with a normal temperature, a heart rate of 86 beats per minute (bpm) and a blood pressure of 124/70 mmHg. The patient’s initial cardiovascular, respiratory and abdominal examination findings were normal, and he exhibited severe depression. The initial laboratory workup showed a sodium level of 137 mEq/L, a potassium level of 4.2 mEq/L, a chloride level of 107 mEq/L, a bicarbonate level of 23 mEq/L and a serum creatinine level of 1.0 meq/L with an estimated creatinine clearance of 95 ml/min/m². The thyroid stimulation hormone (TSH) level was 1.2 pg/mL, the levels of serial cardiac markers were normal and the lithium level was <0.2 mmol/L. The patient was admitted to the psychiatry inpatient unit and administered lithium at a dose of 600 mg three times a day. Approximately four hours after the initial dose of lithium, the patient experienced dizziness with confusion associated with periods of severe bradycardia ranging from a heart rate (HR)
of 28 to 45 bpm. Elektrokardiogramm (EKG) showed a heart rate of 38 beats per minute with an incomplete right bundle branch block (Fig. 1). The patient’s heart rate responded to 0.4 mg of atropine administered intravenously and improved to 64 beats per minute. Subsequently, the patient was monitored on telemetry and the lithium was discontinued. The patient remained asymptomatic and his heart rate normalized without any further episodes of bradycardia. The repeat EKG is shown in Fig. 2. To exclude the presence of structural heart disease, transthoracic echocardiogram was performed, which was found to be normal. In view of the complete recovery of the patient’s heart rate, an electrophysiological study was deferred. The medication regimen was then changed to sodium valproate for bipolar disorder. A gradual improvement was observed in the patient’s depressive symptoms, and he was discharged to home on day 12 of admission without any further complications.

#### Discussion

Lithium is a drug with a narrow therapeutic window and thus requires close monitoring in patients receiving chronic administration (1-3). Following an oral dose of lithium, the achieve peak levels are achieved in two to four hours and the medication is fully absorbed in eight hours (4). The renal clearance of lithium is proportional to its plasma concentration. Approximately 50% of a single dose of lithium is excreted in 24 hours. The major cardiovascular side effects of lithium include unmasking of Brugada syndrome, sinus node dysfunction, atrio-ventricular (AV) block and various arrhythmias (5, 6). Asymptomatic electrocardiographic changes are commonly observed, specifically, changes in T waves characterized by flattening, isoelectrical changes or inversion. These changes have a reported incidence varying from as low as 20% to 30% up to 100%. Although most side effects occur at the supratherapeutic levels, there are several case reports of conduction abnormalities induced by lithium in patients at levels within the therapeutic range (0.6-1.2 meq /L) (1, 2). This suggests a wide range of individual responsiveness to lithium.

There are various mechanisms by which lithium is postulated to cause conduction abnormalities. Animal studies have shown that lithium can cause displacement of intracellular potassium thereby leading to hyperkalemia, which further causes arrhythmias (7). Other animal studies have shown that lithium decreases both the spontaneous rate of depolarization of the sinus node and the conduction velocity in the atrioventricular and intraventricular conduction system (8). These electrophysiological effects of lithium might account for the lithium-induced sinus nodal dysfunction observed in humans. Other possible mechanisms include a reduced response to adrenergic stimulation (9), prolongation of effective refractory period of the atrium (10), interference with calcium ion influx in pacing cells of the sinus node (11) and the blocking of cardiac sodium channels (12).

Rosenqvist and colleagues concluded in their study that long-term lithium treatment changes the ionic milieu within spontaneously depolarizing sinus node cells, even at therapeutic concentrations (11). However, our case shows that even a single dose can lead to severe symptomatic bradycardia. This may possibly occur secondary to a higher level occurring transiently after a single dose. This case also highlights the important need to consider individual responsiveness to lithium, as the response may vary from person to person. Our case represents a unique situation in which a single dose of lithium caused the patient to develop severe symptomatic bradycardia. To the best of our knowledge, this is the first case of this phenomenon reported in the literature.

Previous studies have shown better tolerance with lithium when dosed on a once-daily dosing schedule. This case highlights the need for vigilance when administering lithium, possibly more so when giving a higher dose once daily. Performing resting electrocardiogram, assessing the renal function with regular periodic examinations of the lithium levels and monitoring the pulse rate is effective for the early detection of potentially serious side effects of lithium. As suggested by a previous review, in cases of side effects, prompt discontinuation of lithium therapy is advised (13). However, if severe bradycardia occurs, atropine can be administered emergently, and temporary pacing can be considered for persistent bradycardia.

The authors state that they have no Conflict of Interest (COI).
References


© 2013 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imonline/index.html